

### 1054-20 Vulnerable Plaque Characterization With Intravascular Elastography

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**Background:** The cap of a vulnerable plaque is the weakest link, which can rupture due to increased strain. Intravascular elastography is a new technique to measure local strain in a plaque. Up to now it was unknown, how plaque morphology and strain patterns correspond.

**Methods:** Diseased coronary artery specimens, collected after autopsy, were evaluated for their morphological properties with standard intravascular ultrasound catheters and an elastographic workstation in a water-tank at different intraluminal pressures (80 and 100 mmHg).

Selected segments were stained on the presence of collagen and fat, smooth muscle cells and macrophages. In histology a vulnerable plaque was defined as plaque with a thin cap with moderate/heavy macrophage infiltration and a plaque that consisted for at least 40% of atheroma. In elastography, vulnerable plaque was defined as a high strain region on the surface of the plaque with an adjacent low strain region. In every cross-section a most dangerous part was defined as the part with the highest strain and compared to the underlying histology. Observers blinded for the outcome of the other technique, analyzed elastograms and histology.

**Results:** In 24 diseased coronary arteries, we studied 54 crosssections. 23 vulnerable plaques and 31 non-vulnerable plaques were found. There was a high correlation ( $p = 0.0001$ ) between the relationship of strain in the plaque and presence of macrophages. Furthermore there is an inverse relationship between strain and amount of smooth muscle cells ( $p = 0.031$ ). Plaques, which are declared vulnerable in elastography, have a thinner cap than non-vulnerable plaques and a higher amount of macrophage staining ( $p = 0.01$ ).

**Conclusion:** Intravascular elastography detects high strain regions in vulnerable plaques, which correlate with an infiltration of macrophages in caps and a decreased amount of smooth muscle cells. Elastographically vulnerable plaques have a thinner cap than non-vulnerable plaques.

## POSTER SESSION

### 1055 Cellular Markers of Restenosis

Sunday, March 17, 2002, 3:00 p.m.-5:00 p.m.

Georgia World Congress Center, Hall G

Presentation Hour: 3:00 p.m.-4:00 p.m.

### 1055-21 Expression of Lectin-Like LDL Receptor (LOX-1) in Smooth Muscle Cells After Balloon Injury

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**Background:** Lectin-like oxidized LDL receptor-1 (LOX-1) was originally isolated as an oxidized LDL receptor in endothelial cells. Recently, it was reported that LOX-1 was highly expressed in intimal smooth muscle cells (SMC), as well as macrophages, in advanced human atherosclerotic lesions. However, LOX-1 expression in restenosis after vascular balloon injury has not been explored. Therefore, we investigated the expression of LOX-1 in the neointima and media of rabbit aortas after balloon injury.

**Methods:** Endothelium of rabbit aortas was denuded three times with a balloon catheter. Aortas were removed at 6, 12, and 24 hours, 2, 5, and 7 days, and 2, 4, 8, 16, and 24 weeks after the balloon injury. Expression of LOX-1 protein was analyzed by immunohistochemistry using a specific monoclonal antibody directed to rabbit LOX-1. LOX-1 mRNA was measured by a quantitative reverse transcription polymerase chain reaction (RT-PCR) and in situ hybridization.

**Results:** RT-PCR revealed that LOX-1 mRNA was undetectable in non-injured aortas (control). In balloon-injured aortas, in contrast, LOX-1 mRNA began to be expressed at 6 hours, peaked at 2 to 5 days (a 8.5-fold increase compared to control), and remained to be expressed at 24 weeks (a 4-fold increase compared to control) after the balloon injury. Immunohistochemical staining showed that LOX-1 protein was not detected in non-injured aorta and appeared in medial SMC at 2 days after injury, before the formation of neointima. At 5 days after the balloon injury, neointima formation is detectable and LOX-1 protein was expressed in both medial and neointimal SMC. LOX-1 protein continued to be expressed until 24 weeks after vascular injury in medial and neointimal SMC. In situ hybridization also showed similar time-dependent LOX-1 mRNA expression in both medial and neointimal SMC after the balloon injury.

**Conclusion:** LOX-1 was induced in both medial and neointimal SMC after vascular injury, suggesting that LOX-1 plays an important role in restenosis after vascular injury.

### 1055-22 Immunohistochemical Staining of C-Reactive Protein Predicts Restenosis After Directional Coronary Atherectomy in Patients With Angina Pectoris

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**Background:** Recent evidence suggests that plasma levels of C-reactive protein (CRP) may be a reliable marker of the risk of restenosis after percutaneous coronary intervention. Moreover recently, it has been reported that levels of both CRP mRNA and protein are increased in postmortem arterial plaque tissue. We investigated whether late outcome after directional coronary atherectomy (DCA) could be predicted by CRP staining in DCA samples. **Methods:** We examined CRP immunoreactivity in 28 DCA samples (22 samples from primary lesion, 6 samples from restenotic lesion) from 24 patients with angina pectoris. Restenosis, defined as  $>50\%$  stenosis diameter by quantitative cineangiography, was present in 15 samples, whereas remaining 13 samples ( $<50\%$  stenosis) showed no restenosis. We counted the density (number/mm<sup>2</sup>) of total cells, SMCs, macrophages and CRP positive cells. **Results:** CRP immunoreactivity localized to smooth muscle cells (SMCs) and macrophages. The ratio of SMCs and macrophages to total cells were similar in samples from patients with and without restenosis ( $42 \pm 13\%$  and  $42 \pm 17\%$ ,  $17 \pm 10\%$  and  $19 \pm 12\%$ , respectively). However, the ratio of CRP positive cells to total cells was significantly higher in DCA samples from patients with restenosis than without restenosis ( $20 \pm 9.4\%$  vs.  $10 \pm 6.1\%$ ,  $P < 0.01$ ). In addition, the ratio of CRP positive cells significantly correlated with late luminal loss ( $R = 0.526$ ,  $P < 0.01$ ) and loss index ( $R = 0.683$ ,  $P < 0.0001$ ) after DCA. **Conclusions:** CRP immunopositivity in resected coronary atheromatous tissue is a powerful predictor of restenosis after DCA, suggesting that CRP may play a role in the restenotic process after percutaneous coronary intervention.

### 1055-23 Increased Peroxisome Proliferator-Activated Receptor Gamma (PPAR) Expression in Atherectomy Specimens From Patients With Restenosis After Percutaneous Transluminal Coronary Angioplasty

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**Background:** PPAR is a member of the nuclear receptor superfamily of ligand-activated transcription factors, and it has been reported that monocytes/macrophages in human atherosclerotic lesions express immunostained PPAR. However, the role of PPAR in restenosis after coronary intervention is unexplored. In the present study, we examined the PPAR expression of atherectomy specimens by immunohistochemical analysis. **Methods:** Atherectomy samples were obtained from 15 patients with restenosis after PTCA and 15 patients with de novo lesions of stable exertional angina by directional coronary atherectomy. Immunohistochemical staining was performed on serial sections using monoclonal antibodies against PPAR, macrophages and smooth muscle cells (SMCs). **Results:** There were no significant differences in patients characteristics of the age, sex, and coronary risk factors between the restenosis and the stable exertional angina groups. PPAR immunoreactivity was found in all restenotic lesions obtained from patients after PTCA and was in 8 of the 15 patients in de novo lesions from patients with stable exertional angina. Moreover, there was higher density of PPAR immunostaining in restenotic lesions than in de novo sites. In restenotic lesions, neointimal thickening contained macrophages but was composed predominantly of SMCs, and in terms of the cellular types, SMCs and macrophages expressed PPAR. Especially, immunopositive SMCs for PPAR were strongly observed around macrophages infiltration in restenotic sites. In de novo lesions, there was less immunoreactivity of PPAR on macrophages and SMCs compared with restenotic sites. **Conclusions:** We have shown that the expression of PPAR was more frequently observed in restenotic lesions after PTCA than in de novo lesions obtained from the patients with stable exertional angina by immunohistochemistry. These results indicate that local expression of PPAR may be associated with the mechanisms of vascular remodeling after coronary intervention.

### 1055-24 Pregnancy Associated Plasma Protein-A Is Preferentially Expressed in Plaque of Patients With Restenosis

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**Background:** Insulin like growth factor-1 (IGF) is abundantly expressed in atherosclerotic and restenotic human arteries and is regulated by IGF binding proteins. Recently, pregnancy associated plasma protein (PAPP-A) has been identified as an IGF binding protein-4 protease associated with the injury/repair response. We sought to determine the expression of PAPP-A in human atherosclerosis specimens obtained by directional atherectomy (DCA) and its relationship with the clinical presentation of the patient.

**Methods:** DCA specimens from 89 patients (pts) were immunostained for PAPP-A. The slides were then blindly read for the presence and extent of PAPP-A staining. PAPP-A presence was semi-quantitatively analyzed. Clinical data were extracted from the charts and cardiac catheterization laboratory database.

**Results:** The study group consisted of 71/89 males, mean age  $64 \pm 11$  years, 37/89 pts had acute coronary syndromes, 16/89 had myocardial infarction, 27/89 had restenotic lesions and 13/89 had diabetes. Sixty-two percent of the DCA specimens expressed PAPP-A. The patients with restenotic lesions had statistically higher PAPP-A scores than the other pts, as did pts with diabetes. (See figure)

**Conclusions:** PAPP-A is expressed in most DCA specimens and shows increased